08/468161

**UNITED STATES DEPARTMENT OF COMMERCE**
**Patent and Trademark Office**
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| SERIAL NUMBER | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 08/468,161 | 06/06/95 | DEFEO-JONES D | 192531B |

18N2/0203

DAVID A MUTHARD
PATENT DEPARTMENT
MERCK & CO INC
PO BOX 2000
RAHWAY NJ 07065-0907

| EXAMINER | |
|---|---|
| MARSCHALL C | |
| **ART UNIT** | **PAPER NUMBER** |
| 1811 | 6 |

**DATE MAILED:** 02/03/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☑ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

**Part II SUMMARY OF ACTION**

1. ☑ Claims 1-20 are pending in the application.
   Of the above, claims 8-11 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-7, 12-20 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

**EXAMINER'S ACTION**

**Part III DETAILED ACTION**

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 1-7 and 12-20 are, drawn to oligopeptide and conjugates, classified in Class 530, subclass 324,326,328-329 and 402.

Group II. Claims 8-11, drawn to assay, classified in Class 435, subclass 1+.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions of Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product as claimed can be used as in methods of treating prostatic cancer.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, different search and recognized divergent subject matter restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Mr. David Muthard on January 29 1997 a provisional election was made with traverse to prosecute the invention of Group 1 claims 1-7, 12-20 . Affirmation of this election must be made by applicant in responding to this Office action. Claims 8-11 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle*

*Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 5-6 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1,5-6 of copending application Serial No. 08/267,092, which has been allowed. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending application Serial No. 08/540412. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting

ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-4 of copending application Serial No. 08/267,092 which has been allowed. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter in both application is co-extensive.
This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 2-7, 12-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-7, 12-23 of copending application Serial No. 08/540412. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter is co-extensive.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lilja et al (Journal of Biological Chemistry, vol, 264, No.3, pp 1894-1900).

The instant invention relates to oligopeptides which are enzymatically cleaved by active free prostate specific antigen.

Since applicants' claims use the terminology "comprises", applicants' peptides encompass the entire sequence of semenogelin (See Lilja et al, supra Fig.2, p. 1897). Sememogelin contains three cleavages sites(See Fig 2, p. 1897).

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claim 7 is rejected under 35 U.S.C. § 103 as being unpatentable over Lilja et al, supra in view of Applicants' Admission.

As previously stated in the discussion under 35 USC 102(b), the peptide of the instant invention reads on the entire amino sequence of semenogelin. However, the reference of Lilja et al differs from the peptide of claim 7 in that Lilja et al does not teach that their peptides can be protected at the N with acetyl or amidated C terminus . As stated by applicants, it is well

known in the chemical art that protection of the amino moiety with acetyl, benzoyl, pivaloyl and the like reduces or eliminates the enzymatic degradation of such peptidyl therapeutic agents by the actio n of exogenous amino peptidases which are present in the blood plasma of warm blooded animals (See spec., p.39). It is also well known in the art that amide form of the instant peptide also reduces or eliminates enzymatic degradation of such peptidyl therapeutic agents.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 12-20 are rejected under 35 U.S.C. § 103 as being unpatentable over Lilja et al in view of Kaneko et al.

Lilja et al teach polypeptides that read on the instant invention, however Lilja et al do not teach that the instant peptides are conjugated to any cytotoxic agents.

The instant invention relates to oligopeptides which comprise teh amino acid sequences that are recognized and proteolytically cleaved by free prostate specific antigen. The oligopeptides are useful in assays which can determine the free PSA protease activity in vitro and invivo. The oligopeptides may be incorporated into therapeutic agents which conjugates of such oligopeptides and known cytotoxic agents and which are useful in the treatment of prostatic cancer.

Nevertheless, the reference of Kaneko et al also discloses anthracycline-ligand conjugates comprised of a ligand that reacts with one or more receptors associated with the cell surface of a target cell population, the ligand having at least one anthracycline derivative-molecule linked to it structure (see col.10, lines 19-43). The cytotoxic reagents may be any molecule containing a carbonyl group. Such reagents include but are not limited to, the anthracyclines(see col 10,lines 50-60). Therefore, it would have been obvious to one of ordinary skill in the art at the time that the invention was made to modify the polypeptide of Lilja et al by conjugating it to one of anthracyclines so as to prepare anthracycline-oligopeptide conjugates that are useful in the treatment of prostatic cancer.

The references of Priest and Lilja et al are further cited to show the state of the art and were made of record in the parent cases and will not be provided to applicants.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Marshall whose telephone number is (703) 308-1030.

sgm
January 30, 1997

Avis M. Davenport

AVIS M. DAVENPORT
PRIMARY EXAMINER
GROUP 1800